

**WHAT IS CLAIMED IS:**

1. A method of assaying the functionality of a translation product of a mutant  $\Delta\text{TR}\alpha 2$  gene in a cell, the method comprising binding a labeled  $\Delta\text{TR}\alpha 2$  ligand to the translation product in a cell and measuring the amount, location, or rate of transit of the ligand in the cell, wherein an increase in the amount, location, or rate of transit of the ligand in the cell compared to that in a cell that does not comprise a mutant  $\Delta\text{TR}\alpha 2$  gene indicates an increase in functionality of the translation product, and a decrease in the amount, location, or rate of transit of the ligand in the cell compared to a cell that does not comprise a mutant  $\Delta\text{TR}\alpha 2$  gene indicates a decrease in the functionality of the translation product.
2. The method of claim 1, wherein the ligand is a flavone.
3. The method of claim 1, wherein the ligand is an aurone.
4. The method of claim 1, wherein the ligand is a T4 analog.
5. A method of identifying a candidate compound that modulates  $\Delta\text{TR}\alpha 2$  polypeptide activity, the method comprising:
  - a) obtaining a  $\Delta\text{TR}\alpha 2$  polypeptide
  - b) contacting the  $\Delta\text{TR}\alpha 2$  polypeptide with a test compound, and
  - c) assaying for binding of the test compound to the  $\Delta\text{TR}\alpha 2$  polypeptide, wherein binding indicates that the test compound is a candidate compound.
6. A method of identifying a candidate compound that modulates  $\Delta\text{TR}\alpha 2$  polypeptide activity, the method comprising:
  - a) obtaining a  $\Delta\text{TR}\alpha 2$  polypeptide bound to a  $\Delta\text{TR}\alpha 2$  ligand,
  - b) contacting the  $\Delta\text{TR}\alpha 2$  polypeptide bound to the  $\Delta\text{TR}\alpha 2$  ligand with a test compound, and

c) measuring the displacement of the  $\Delta\text{TR}\alpha 2$  ligand from the  $\Delta\text{TR}\alpha 2$  polypeptide, wherein displacement indicates that the test compound is a candidate compound that modulates  $\Delta\text{TR}\alpha 2$  polypeptide activity.

7. A method of identifying a candidate compound that modulates  $\Delta\text{TR}\alpha 2$  polypeptide activity, the method comprising:

- a) obtaining a test sample containing a  $\Delta\text{TR}\alpha 2$  polypeptide,
- b) incubating the test sample with a test compound, and
- c) assaying the test sample containing the test compound for an alteration in type II 5' deiodinase (D2) activity, such that a test compound that alters D2 activity when compared to a test sample that was not incubated with the test compound is a candidate compound.

8. The method of claim 7, wherein the test compound decreases the amount of D2 activity.

9. A method of identifying a candidate compound that modulates  $\Delta\text{TR}\alpha 2$  polypeptide activity, the method comprising:

- a) obtaining a test sample containing a  $\Delta\text{TR}\alpha 2$  polypeptide,
  - b) performing an actin binding assay with the test sample in the presence of a test compound,
- such that a test compound that alters the binding of p29 vesicles to F-actin when compared to a test sample that was not incubated with the test compound is a candidate compound.

10. The method of claim 5, wherein the test compound is a flavone.

11. The method of claim 6, wherein the test compound is a flavone.

12. The method of claim 7, wherein the test compound is a flavone.

13. The method of claim 9, wherein the test compound is a flavone.

14. The method of claim 5, wherein the test compound is an aurone.

15. The method of claim 6, wherein the test compound is an aurone
16. The method of claim 7, wherein the test compound is an aurone
17. The method of claim 9, wherein the test compound is an aurone
18. The method of claim 5, wherein the test compound is a T4 analog.
19. The method of claim 6, wherein the test compound is a T4 analog.
20. The method of claim 7, wherein the test compound is a T4 analog.
21. The method of claim 9, wherein the test compound is a T4 analog.
22. A compound identified by the method of claim 5.
23. A compound identified by the method of claim 6.
24. A compound identified by the method of claim 7.
25. A compound identified by the method of claim 9.
26. A method of treating a subject who has a neurologic disorder, the method comprising administering to the subject a therapeutically effective amount of a  $\Delta\text{TR}\alpha 2$  ligand.
27. A method of treating an individual who has a mood disorder, the method comprising administering to the individual a therapeutically effective amount of a  $\Delta\text{TR}\alpha 2$  ligand.
28. An isolated nucleic acid molecule comprising a  $\Delta\text{TR}\alpha 2$  targeting construct comprising a DNA sequence homologous to a sequence encoding a mouse  $\Delta\text{TR}\alpha 2$  polypeptide, wherein when the construct is introduced into a mouse cell or an ancestor of the mouse cell at an embryonic stage, and the construct-derived sequences are incorporated into an endogenous  $\text{TR}\alpha$  gene, the cell does not express  $\Delta\text{TR}\alpha 2$  in significant amounts.

29. A vector comprising the nucleic acid of claim 28.
30. The isolated nucleic acid molecule of claim 28, wherein the construct comprises a nucleic acid sequence homologous to intron 7 of a mouse TR $\alpha$  gene.
31. The isolated nucleic acid molecule of claim 28, wherein introduction of the construct disrupts the AP1, ctf, GR, SP1, or ets1 sequence of intron 7.
32. The isolated nucleic acid molecule of claim 28, further comprising a gene selection cassette.
33. The isolated nucleic acid molecule of claim 28, wherein the construct comprises a nucleic acid sequence homologous to exon 10 of a mouse TR $\alpha$  DNA sequence.
34. A transgenic, non-human animal whose germ cells and somatic cells comprise a mutated TR $\alpha$  gene, the mutation being sufficient to inhibit binding of thyroxine (T4) to  $\Delta$ TR $\alpha$ 2 transcribed from the gene, said mutated gene being introduced into the non-human animal or an ancestor of the animal at an embryonic stage, wherein the animal, if homozygous for the mutation, has impaired motor function.
35. A transgenic, non-human animal of claim 34, wherein the animal is a mouse or a rat.
36. A transgenic, non-human animal of claim 34, wherein the animal is a goat, sheep, or a pig.
37. A cell derived from the animal of claim 34.
38. The cell of claim 37, wherein the cell is an astrocyte.
39. The transgenic animal of claim 34, wherein the TR $\alpha$  gene is mutated in intron 7.

